# PATENT COOPERATION TREA

From the INTERNATIONAL SEARCHING AUTHORITY

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## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(date/month/year)* 08 March 2005 (08-03-2005)

Applicant's or agent's file reference
08898996WO

**FOR FURTHER ACTION**
See paragraph 2 below

| International application no | International filing date *(date/month/year)* ) | Priority date *(date/month/year)* |
|---|---|---|
| PCT/CA2004/001940 | 09 November 2004 (09-11-2004) | 12 November 2003 (12-11-2003) |

International Patent Classification (IPC) or both national classification and IPC

A61L-27/28, A61L-27/54, A61P-35/00 A61P-31/00 A61P-31/12 A61F-2/01 A61L-27/38 A61K-35/14 A61F-2/02 A61L-27/34

Applicant KEENAN, JAMES

1. This opinion contains indications relating to the following items :

| | | |
|---|---|---|
| [x ] | Box No. I | Basis of the opinion |
| [ ] | Box No. II | Priority |
| [x ] | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| [ ] | Box No. IV | Lack of unity of invention |
| [x ] | Box No. V | Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| [ ] | Box No. VI | Certain documents cited |
| [ ] | Box No. VII | Certain defects in the international application |
| [x ] | Box No. VIII | Certain observations on the international application |

2. **FURTHER ACTION**
If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/CA
*Commissioner of Patents*
*Canadian Patent Office*
*Box PCT, Ottawa/Gatineau K1A 0C9*

Authorized officer

Stephen Decker (819) 934-2333

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/CA2004/001940

**Box No. I Basis of this opinion**

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language which it was filed, unless otherwise indicated under this item.

[ ] This opinion has been established on the basis of a translation from the original language into the following language __, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of :

a. type of material

[ ] a sequence listing

[ ] table(s) related to the sequence listing

b. format of material

[ ] in written format

[ ] in computer readable from

c. time of filing/furnishing

[ ] contained in the international application as filed.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority for the purposes of search.

3. [ ] In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments :

**WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY**

International application No.
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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of :

[ ] the entire international application

[x ] claims Nos. 37 and 45-55

because

[x ] the said international application, or the said claims Nos. 37 and 45-55 relate to the following subject matter which does not require an international preliminary examination *(specify)* :

claim 37 is directed to a method of treatment of the human or animal body (Rule 39.1 (iv) PCT);
claims 45-55 are also directed to a method of treatment of the human or animal body (Rule 39.1 (iv) PCT), however, the search was carried out on the alleged effects of the device.

[ ] the description, claims or drawings *(indicate particular elements below)* or said claims Nos. ___ are so unclear that no meaningful opinion could be formed *(specify)* :

[ ] the claims, or said claims Nos. ___ are so inadequately supported by the description that no meaningful opinion

[x ] no international search report has been established for said claim No. 37 .

[ ] the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that :

| | | |
|---|---|---|
| the written form | [ ] | has not been furnished |
| | [ ] | does not comply with the standard |
| the computer readable form | [ ] | has not been furnished |
| | [ ] | does not comply with the standard |

[ ] the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

[x ] See Supplemental Box for further details.

**WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY**

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**Box No. V reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Claims | 4, 5, 7, 11, 12, 16-33, 38-44 and 47-55 | YES |
| | Claims | 1-3, 6, 8-10, 13-15, 34-36, 45 and 46 | NO |
| Inventive step (IS) | Claims | 4, 5, 7, 16, 22-25, 32, 33, 39, 41, 50 and 53 | YES |
| | Claims | 1-3, 6, 8-15, 17-21, 26-31, 34-36, 38, 40, 42-49, 51, 52, 54 and 55 | NO |
| Industrial applicability (IA) | Claims | 1-36 and 38-44; 37 and 45-55 (see Supplemental Box V) | YES |
| | Claims | | NO |

2. Citations and explanations :

D1 US 4732155 (ZETTER, B. R. et al.) 22 March 1988 (22.03.1988)
D2 CA 2178541 (FEARNOT, N. E. et al.) 08 December 1996 (08.12.1996)
D3 WO 03/061718 (SHEPARD, D. C. et al.) 31 July 2003 (31.07.2003)
D4 WO 03/022360 (HANDY, E. S. et al.) 20 March 2003 (20.03.2003)
D5 CA 2434320 (VICARI, A. P. et al.) 01 August 2002 (01.08.2002)
D6 US 6366808 (SCHROEPPEL, E. A. et al.) 02 April 2002 (02.04.2002)

The document D1 discloses a medical implant device comprising a polymer matrix impregnated with a chemoattractant agent that acts to attract and retain diseased cells from the environment surrounding the implant device. The chemoattractant agent is selected from a list including: histamine, tuftsin, peptides of specific amino acid residues, collagen type I, epidermal growth factor, endotoxin standard, prostaglandin E and heparin. In a preferred embodiment the chemoattractant is stored in a reservoir attached to a pump which allows continual release of the chemoattractant over a long period of time and permits refilling of the reservoir.

The document D2 discloses a medical implant device coated with a therapeutic agent for the localized delivery of said therapeutic agent at the implantation site. The therapeutic agent is selected from a list including: chemotherapeutic agents, radiotherapeutic agents, radiolabelled agents, antiviral agents, antimicrobial agents, antibiotic agents, and antimitotic agents. In a preferred embodiment the implant device is a vascular stent coated first with a layer of a therapeutic agent and subsequently coated with a polymeric layer to prevent degradation of the therapeutic agent and to enable controlled release of the therapeutic agent.

The document D3 discloses a medical implant device coated with a therapeutic enzyme for the localized delivery of said enzyme at the implantation site. In a preferred embodiment the implant device is a vascular stent or graft coated with a therapeutic enzyme to deliver localized treatment of diseased cells in the vascular system.

The document D4 discloses a therapeutic method for the treatment of disease whereby a magnetic composition comprising ferromagnetic particles attached to a target-specific ligand is administered to a patient followed by the application of an alternating magnetic field to inductively heat and degrade the targeted disease cells. In a preferred embodiment the target cells are cancer cells and the target specific ligand is a chemokine which selectively binds to the diseased cancer cells.

The document D5 discloses the use of chemokines to facilitate the migration of dendritic cells to a localized treatment site to enhance the immune response of the individual. An antigen selected from a list including: tumour-associated antigens, viral antigens, bacterial antigens and fungal antigens can also be administered in conjunction with the chemokine to further enhance the immune response.

The document D6 discloses a medical implant device for the localized delivery of electrochemotherapy for the treatment of cancerous tumours. The implant device employs a variety of levels of electric fields and currents either alone or in conjunction with traditional chemotherapy agents to reduce the size of cancerous tumours.

Continued in Supplemental Box.

**WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY**

International application No.
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**Box No. VIII** **Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made :

Claims 1, 38, 45, 47 and 49 do not comply with Article 6 PCT as the term "capable" makes the definition of the implant device indefinite.

Claim 5 does not comply with Article 6 PCT as there is no support in the description for the implant device to further comprise a host cell, an organ cell, osseous tissue, a biotherapeutic or a chemical to create an environment suitable for cell proliferation.

Claims 5, 7, 14, 17 and 31 do not comply with Article 6 PCT as the term "including" makes the definition of the implant device indefinite.

Claim 7 does not comply with Article 6 PCT as the terms "modified" and "enhance" are vague and indefinite.

Claim 8 does not comply with Article 6 PCT as there is no support in the description for the attractant to be a bacterial toxin.

Claims 11, 12, 24, 28, 39, 42, 44 and 52 do not comply with Article 6 PCT as the term "includes" makes the definition of the implant device indefinite.

Claim 22 does not comply with Article 6 PCT since it is unclear how the therapeutic agent can comprise a mechanical means.

Claim 27 does not comply with Article 6 PCT as there is no support in the description for the means for stimulating an immune response to be an interferon, a chemokine or a foreign chemical substance.

Claim 27 does not comply with Article 6 PCT as the term "effective amount" makes the definition of the implant device indefinite.

Claims 34-36 do not comply with Article 6 PCT. The double inclusion of an element makes the claims ambiguous. The term "implant device" [claims 34-36, line 1] has already been defined in the claim, hence, this term should be referred to using a definite article.

Claim 37 does not comply with Article 6 PCT as there is no support in the description for the subject matter of claim 37.

Claims 52-55 does not comply with Article 6 PCT. The claims pertain to an implant device, however, they ultimately reference claim 49 which defines a method of attracting circulating cells and foreign substances. This inconsistency makes the subject matter of the claims unclear and should be removed.

Claims 52-55 does not comply with Article 6 PCT as there is no support in the description for the subject matter of these claims.

**Supplemental Box**

**In case the space in any of the preceding boxes is not sufficient.**

Continuation of : Box III

Claim 37 pertains to a surgical procedure for which the end result could not be deduced. Hence, no search could be carried out based on the alleged effects of the procedure.

Continuation of : Box V

The problem addressed by the present invention is the isolation of circulating diseased or foreign (viral, bacterial, parasitic or other microbial) cells from body fluid channels. The problem was solved through the use of a medical implant device that is fixed to the walls of the channel to which an attractant agent is associated in some fashion. The attractant agent attracts diseased or foreign cells circulating in the body fluid channel which pass through the frame of the implant device. The implant device can further incorporate a therapeutic agent to degrade the cells captured by the attractant agent.

The closest prior art is D1, which discloses a medical implant device comprising a polymer matrix impregnated with a chemoattractant agent to attract and trap circulating diseased cells. The chemoattractant agent is selected from a list including: histamine, tuftsin, peptides of specific amino acid residues, collagen type I, epidermal growth factor, endotoxin standard, prostaglandin E and heparin. In a preferred embodiment the chemoattractant is stored in a reservoir attached to a pump which enables continual release of the chemoattractant over a long period of time and allows the reservoir to be refilled. Hence, the subject matter of claims 1-3, 6, 8-10, 13-15, 34-36, 45 and 46 lack novelty in view of D1 (Article 33(2) PCT).

Document D1 differs from the subject matter of claims 17-21, 30, 31, 38, 43, 47-49 and 51 due to the lack of a therapeutic agent present in the implant to degrade the diseased cells captured by the attractant agent. However, the coating of medical implant devices with therapeutic agents for localized delivery of said therapeutic agents at the implantation site is known in the art as exemplified by documents D2 and D3. The document D2 discloses a medical implant device coated with a therapeutic agent selected from a list including: chemotherapeutic agents, radiotherapeutic agents, radiolabelled agents, antiviral agents, antimicrobial agents, antibiotic agents, and antimitotic agents. The document D3 discloses a vascular implant coated with a therapeutic enzyme for localized delivery of said enzyme at the implantation site. Armed with the combined teachings of D1 with D2 or D3 it would have been obvious to the skilled worker to incorporate a therapeutic agent into the attractant-associated implant device in order to degrade the diseased cells captured by the attractant. Accordingly, the subject matter of claims 17-21, 30, 31, 38, 43, 47-49 and 51 does not involve an inventive step (Article 33(3) PCT).

The difference between document D1 and the subject matter of claims 11, 12, 28, 29, 40, 42-44, 52 and 54 is the inclusion of a magnetic species as a component of the attractant agent or the therapeutic agent. However, the document D4 discloses the use of ferromagnetic particles attached to disease-targeting chemokines for the localized treatment of diseased cells, such as cancer cells. In said treatment the ferromagnetic particles bind to the target diseased cells via the chemokine. The bound diseased cells are then destroyed through inductive heating by the application of alternating magnetic fields. Armed with the combined teachings of D1 and D4 it would have been obvious to the skilled worker to incorporate a magnetic component into the attractant or the therapeutic agent to induce degradation of the diseased cells captured by the attractant. Accordingly, the subject matter of claims 11, 12, 28, 29, 40, 42-44, 52 and 54 does not involve an inventive step (Article 33(3) PCT).

The difference between document D1 and the subject matter of claims 26 and 27 is the use of an immune response stimulating agent as the therapeutic agent. However, the document D5 discloses the use of chemokines in conjunction with antigens to amplify an individuals immune response to disease by facilitating migration of dendritic cells to a localized treatment site. Armed with the combined teachings of D1 and D5 it would have been within the purview of the skilled worker to utilize an immune response stimulating agent, such as an antigen, in conjunction with the attractant-associated implant device to promote degradation of the captured diseased cells. Accordingly, the subject matter of claims 26 and 27 does not involve an inventive step (Article 33(3) PCT).

The difference between document D1 and the subject matter of claims 52 and 55 lies in the use of an external electrical energy source as the therapeutic agent. However, the document D6 discloses a medical implant device that employs a variety of levels of electric fields and currents for the localized delivery of electrochemotherapy to cancerous tumours. Armed with the combined teachings of D1 and D6 it would have been obvious to the skilled worker to employ an electrical energy source as a therapeutic treatment to degrade the diseased cells captured by the attractant-associated implant device. Accordingly, the subject matter of claims 52 and 55 does not involve an inventive step (Article 33(3) PCT).

The subject matter of claims 1-36 and 38-44 is industrially applicable and therefore complies with Article 33(4) PCT.
The subject matter of claims 37 and 45-55 is directed to a method of treatment of the human or animal body (Rule 39.1(iv) PCT). No unified criteria exist in the PCT Contracting States for the assessment of the industrial applicability of claims 37 and 45-55 (Article 33(4) PCT).